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Correlations of Water Quality Parameters with Mutagenicity of Chlorinated Drinking Water Samples

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Adverse health effects that may result from chronic exposure to mixtures of disinfection by-products (DBPs) present in drinking waters may be linked to both the types and concentrations of DBPs present. Depending on the characteristics of the source water and treatment processes used, both types and concentrations of DBPs found in drinking waters vary substantially. The composition of a drinking-water mixture also may change during distribution. This study evaluated the relationships between mutagenicity, using the Ames assay, and water quality parameters. The study included information on treatment, mutagenicity data, and water quality data for source waters, finished waters, and distribution samples collected from five full-scale drinking water treatment plants, which used chlorine exclusively for disinfection. Four of the plants used surface water sources and the fifth plant used groundwater. Correlations between mutagenicity and water quality parameters are presented. The highest correlation was observed between mutagenicity and the total organic halide concentrations in the treated samples.

In the United States, drinking water has been traditionally disinfected with chlorine, greatly reducing the occurrence of waterborne diseases. In addition to disinfection, however, the use of chlorine in water treatment leads to the production of a wide variety of disinfection by-products (DBPs). These by-products result from the reaction of chlorine with naturally occurring materials in surface and ground waters. More than 600 DBPs have been identified in drinking waters, and many by-products remain unidentified (Richardson et al., 2007, 2008; Richardson, 1998). The known by-products account for less than 50% of the mass of total halogenated organics present and the percentage varies from water to water (Richardson, 1998; Wienberg, 1999). Drinking water thus represents a complex mixture to which a large population is exposed on a daily basis.

Drinking-water mixtures vary substantially with regard to both the types and concentrations of DBPs present, depending on the characteristics of the source water and the treatment processes used (Clark et al., 2001). The composition of a drinking-water mixture may also change during the distribution process (Clark et al., 2001; Lebel et al., 1997).

Concern over potential health effects resulting from chronic exposure to the DBPs present in drinking waters has led to numerous epidemiological studies and toxicologic evaluations of individual DBPs formed in drinking waters and of the mixtures of DBPs in drinking waters (Claxton et al, 2008; Richardson et al., 2007; IARC, 2004).

The effects of by-product exposure are assumed to be linked to both the types and concentrations of by-products present (Clark et al., 2001). Therefore, any assessment of the potential adverse health effects associated with drinking water needs to take into account the variability in drinking-water mixtures. Given that adequate chemical and/or toxicological data will not likely be available on every individual drinking water produced, the assessment process could be simplified if drinking waters could be grouped as "sufficiently similar" based on a set of parameters. These parameters would likely include some of the DBPs (or groups of DBPs) themselves, as well as source water characteristics and treatment factors that affect the production of by-products.

A study was conducted to investigate possible relationships between common water quality parameters and mutagenicity. In this study, source waters, finished waters, and distribution samples were collected from five full-scale drinking water treatment plants that used chlorine for disinfection. It was subsequently decided that the data set may also be useful to investigate the "similarity" between drinking-water mixtures.

The views expressed in this paper are those of the individual authors and do not necessarily reflect the views and policies of the U.S. EPA. Those sections prepared by U.S. EPA scientists have been reviewed in accordance with U.S. EPA peer and administrative review policies and approved for presentation and publication. Mention of trade names or commercial products does not constitute endorsement or recommendations for use.

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Data, methods used, and some of the relationships observed are presented here to facilitate the investigation of what constitutes "sufficient similarity" between drinking-water mixtures.

METHODS

Water Treatment

Plant A, sampled in 9/1995, used a groundwater source. Treatment consisted of tray aeration, chlorination, and filtration through sand and gravel (chlorine dose: 2.12 mg/L). Plant B, sampled in 3/1996, used a surface-water source that was stored in a reservoir for 3–4 mo prior to treatment. Treatment consisted of coagulation and pH adjustment (ferric chloride and lime), settling, dual media (anthracite and sand) filtration, and chlorination (added in clearwell). Fluoride and zinc orthophosphate were also added to the water in the clearwell (chlorine dose: 4.1 mg/L). Plant C, sampled in 6/1996, used a surface-water source (a river) that was pumped directly into the plant for treatment. Alum, lime, and chlorine were added to the raw water. The chemical additions were followed by flocculation, clarification, and dual media filtration. Additional chlorine and fluoride were added in a service well prior to clearwell storage (chlorine doses: pre 4.9 mg/L and post 0.4 mg/L).

Plant D, sampled in 9/1997, obtained surface water from a reservoir. Alum, soda ash, and powdered activated carbon were added to the raw water, followed by flocculation and settling. Chlorine was added prior to dual media filtration. Additional chlorine, soda ash, fluoride, and sodium polyphosphate were added to the water in the clearwell (chlorine doses: pre 1.92 mg/L and post 1.98 mg/L).

Plant E, sampled in 9/1998, used surface water from a pond. A coagulating agent was added to the raw water, followed by settling and filtration through dual media. Chlorine and fluoride were then added. Zinc orthophosphate and potassium hydroxide (pH adjustment) were added to the water in the clearwell (chlorine dose: 1.98 mg/L).

Sample Collection

Raw water, finished water, and water samples from the distribution system were collected in 55-gallon stainless-steel drums at each of the drinking-water treatment plants. In some cases, duplicate drums of water were collected in order to verify the reproducibility of the concentration procedures and/or analyses. The water in the drums was sampled the next day for chemical and microbiological analyses. For mutagenicity testing, the organic compounds present in the water samples were concentrated by adsorption on Amberlite XAD resins (Rohm and Haas, Philadelphia, PA).

Sample Concentration

The semivolatile and nonvolatile organic compounds present in the water samples were concentrated for mutagenicity testing by adsorption on XAD resins. Preparation of the resins was described previously (Schenck et al., 1998a). Raw, finished, and distribution water samples (80 L) from each of the plants were concentrated using columns containing 104 ml of each resin, XAD-8 over XAD-2. Immediately prior to passage of the water samples over the columns, the samples were acidified to pH 2 by in-line addition of hydrochloric acid using a metering pump and a static mixer. Previous studies showed the recovery of mutagenic activity to be much greater from water samples acidified to pH 2 prior to passage over XAD columns than from water samples concentrated at pH 8 (Ringhand et al., 1987). The flow rate was 200 ml/min. The columns were eluted with three bed volumes of ethyl acetate. Residual water was removed from the eluates by using separatory funnels to drain off the water layers followed by the addition of sodium sulfate (approximately 8 g/L). The eluates were then concentrated by rotary vacuum evaporation and dissolved in dimethyl sulfoxide (DMSO) to give 8000-fold concentrates.

Assay for Mutagenic Activity

Mutagenic activity was determined in *Salmonella typhimurium* strains TA100 and TA98 with and without metabolic activation, using the standard plate method of Maron and Ames (1983). Strain-specific genetic markers were verified for both strains prior to use. Spontaneous and positive control responses and solvent (100 µl DMSO) controls were included with each assay. In assays using metabolic activation, the methods for preparation of the liver homogenate (S9) from Aroclor 1254-pretreated male Sprague-Dawley rats and the S9 cofactor mix were as described in Maron and Ames (1983). The S9 concentration in the S9 mix was 5% (v/v), and 0.5 ml of S9 mix was added per plate. The positive controls used without S9 were sodium azide for TA100 (1 µg/plate) and 2-nitrofluorene for TA 98 (5 µg/plate). The positive control used with S9 was 2-aminoanthracene for both strains (1 µg/plate). The samples were assayed using at least 6 concentration levels, equivalent to 0.0125–1.6 L per plate, with duplicate plates per concentration. Each sample was assayed two or three times on separate days in TA100 and once in TA98.

Mutagenic activities (expressed as revertants/L equivalent) were determined from the initial slopes of the dose-response curves using the method of Bernstein et al. (1982). Mutagenic activities for a given sample are reported as the average of the slopes determined in separate assays in TA100 without S9.

Chemical Analyses

Total organic carbon (TOC) concentrations were determined using the wet-oxidation method (5310D), and the adsorption–pyrolysis–titrimetric method (5320B) was used for total organic halide (TOX) analyses (Greenberg et al., 1992). Total trihalomethanes (TTHM) were determined by EPA Method 551 (U.S. EPA, 1990). Six of the haloacetic acids (HAA6: chloroacetic acid, bromoacetic acid, dichloroacetic acid,

trichloroacetic acid, bromochloroacetic acid, and dibromoacetic acid) were quantified by EPA Method 552, using the micro-extraction procedure (U.S. EPA, 1990). Ammonia concentrations were determined using the automated phenate method, EPA method 350.1 (U.S. EPA and USGS, 2008). Either EPA Method 300.0 or EPA Method 300.1 was essentially used for the determination of bromide (U.S. EPA and USGS, 2008).

Chlorine dose values were obtained from the treatment plants, and represent the chlorine dose applied on the day that the water samples were collected. The *N,N*-dimethyl-*p*-ferrous phenylenediamine ammonium sulfate titrimetric method (4500-Cl F) was used for determining residual chlorine concentrations (Greenberg et al., 1992).

Assimilable organic carbon (AOC) was determined using a modification of the *Pseudomonas fluorescens* strain P-17, *Spirillum* strain NOX method (9217B) (Greenberg et al., 1992). Heterotrophic bacteria were enumerated on plate count agar (35°C/48 h) using the pour plate method (9215B) (Greenberg et al., 1992).

Statistical Analysis

Pearson product moment correlations were calculated between mutagenicity, as determined in TA100, without S9, and various water quality parameters using data from the raw water, finished water, and distribution samples from each of the treatment plants. The criterion for significance was set at $p < .05$.

RESULTS AND DISCUSSION

Several factors influence the types and concentrations of DBPs present in drinking waters, as well as the levels of mutagenicity observed. These factors include the type of disinfectant used, the concentration of organic matter in the source water, and the presence of bromide.

Four of the plants sampled in this study treated surface water sources using conventional treatment (coagulation, flocculation/settling, filtration). One plant treated a groundwater source. All of the plants used chlorine exclusively for disinfection. Ammonia present in the raw water or added during the treatment process can lessen DBP formation (Clark et al., 2001) and was shown to reduce the level of mutagenicity observed relative to the use of chlorine alone (Cheh et al., 1980; Patterson et al., 1995). All of the plants had either nondetectable levels or relatively low levels of ammonia present in the raw water, as well as in the finished and distribution samples (Table 1), and ammonia was not added during treatment (see Methods).

In this study, the addition of a metabolic activating system (+S9) resulted in decreased levels of mutagenic activity in all of the chlorinated water samples. Additionally, TA100 showed a higher reversion rate than that observed in TA98 for the chlorinated samples. Both of these observations are consistent with previous studies of chlorinated water samples (Cheh, et al., 1980; Grimm-Kibalo, et al., 1981; Miller et al., 1986; Claxton et al, 2008). Consequently, correlations were calculated between mutagenicity, as determined in TA100 without S9, and the water quality parameters evaluated.

Total organic carbon (TOC) is a measurement commonly used to indicate the amount of organic material present in water. Generally, as the concentration of TOC in the source water increases, the concentrations of DBPs increase (Fair, 1995). The levels of mutagenicity produced following chlorination of humic acids, a major component of the organic matter present in natural waters, were also found to rise with increasing TOC (Meier et al., 1983). Consistent with these observations, there is a fairly good correlation ($r = .86$) between the TOC concentrations of the raw waters and the mutagenicity levels (mean revertants/L equivalent) in the finished water samples (Figure 1). The observed correlation between raw water TOC and mutagenicity decreases, however, if the distribution samples are included ($r = .58$). This is likely due to the fact that the level of mutagenicity observed may be affected by distribution. The levels of mutagenicity in several of the distribution samples in this study were significantly different from the finished water collected from the same treatment plant (Schenck et al., 1998a, 1998b). The correlation between raw water TOC and TOX, often used as an estimate of total halogenated by-products, showed a similar pattern. When only the finished water samples are included, $r = .78$. If the distribution samples are included, $r = .58$, suggesting distribution effects.

The studies of Meier et al. (1983), using chlorinated humic acids, also showed that increasing the chlorine to carbon ratio resulted in a rise in the formation of both mutagenic activity and TOX. In the model developed by Vartiainen et al. (1988), the mutagenicity of chlorinated drinking waters is primarily a function of TOC concentration of the source water and the chlorine dose (see also U.S. EPA, 2001). This relationship between the formation of mutagenicity and TOX and the concentrations of carbon and chlorine can also be seen in this study. Figure 2 shows the correlation between mutagenicity and the product of raw water TOC and total chlorine dose in both the finished and distribution samples. The correlation between TOX and the product of raw water TOC and total chlorine dose is similar ($r = .89$).

Correlations between various chemical parameters in the finished and distribution water samples and their levels of mutagenicity were also investigated. The highest correlation observed in this study was between the concentrations of TOX and the mutagenicity levels in the treated water samples (Figure 3). Previous studies of chlorinated drinking waters (Kool et al., 1984; Kito et al., 1988) and chlorinated humic acid solutions (Meier et al., 1983) have also reported high correlations between TOX and mutagenicity.

The concentrations of HAA6 (total concentration of the six quantified haloacetic acids) also showed a good correlation with the levels of mutagenic activity in the treated water samples (Figure 4). This correlation would be higher ($r = .92$),

TABLE 1
Water Quality Data and Mutagenicity of Water Samples

Plant	Sample type	Mutagenicity mean revertants/L[a]	TOC, mg/L	NH_3, mg/L	TOX, µg/L	HAA6, µg/L[b]	TTHM, µg/L	Bromide, mg/L	Percent TTHM, Br only[c]	Percent HAA6, Br only[c]	Percent TTHM, with Br[c]	Percent HAA6 with Br[c]
A	Raw	NS	2.1	0.207	<5	<MDL	<0.1	NA				
A	Finished (A)	875	1.9	<0.036	28	2.4	17	NA	42	68	94	86
A	Finished (B)	1008	2.1	<0.036	26	2.7	17	NA	43	68	94	86
A	Distribution 1 (A)	370	2	<0.036	31	1.1	38	NA	64	62	97	71
A	Distribution 1 (B)	334	1.9	<0.036	33	1.2	40	NA	64	58	97	73
A	Distribution 2	684	2	<0.036	29	4	27	NA	56	73	96	87
B	Raw	NS	5.8	0.036	8	<MDL	<0.1	0.018				
B	Finished	5636	5	0.036	450	98	66	<0.005	0	0.09	9.6	1.6
B	Distribution 1	5556	5.2	<0.036	490	110	82	<0.005	0	0.02	9	1.5
B	Distribution 2	5380	4.9	0.036	490	120	99	<0.005	0	0.07	8.7	1.5
C	Raw	82	2.4	<0.036	<5	<MDL	10	0.016	0		17	
C	Finished	3738	1.7	<0.036	230	65	64	<0.005	4	0.08	18	2.3
C	Distribution 1	5254	3.1	<0.036	460	130	180	<0.005	0	0	3.8	1
C	Distribution 2	3994	1.8	<0.036	200	66	90	<0.005	0	0.08	8	2.4
D	Raw	NS	4.7	<0.036	6	<MDL	<0.1	<0.005				
D	Finished (A)	3562	2.4	<0.036	260	73	100	<0.005	0	0	15	3.9
D	Finished (B)	3566	2.4	<0.036	270	74	84	<0.005	0	0	17	3.9
D	Distribution 1	3615	2.3	<0.036	280	78	99	<0.005	0	0	16	3.7
D	Distribution 2	2773	2.3	<0.036	230	35	120	<0.005	0	0	14	0
E	Raw	132	8	<0.036	26	<MDL	<0.1	0.036				
E	Finished	5731	3.5	<0.036	320	59	72	0.015	3	0.3	21	7.2
E	Distribution 1	3453	3.2	<0.036	290	<MDL	68	0.019	0	0	19	
E	Distribution 2	2977	3.3	<0.036	240	<MDL	78	0.022	0	0	17	

Note. TOC, total organic carbon; TOX, total organic halide; HAA6, six of the haloacetic acids (chloroacetic acid, bromoacetic acid, dichloroacetic acid, trichloroacetic acid, bromochloroacetic acid, and dibromoacetic acid); TTHM, total trihalomethane; NS, not significant; NA, not analyzed.

[a]Revertants per liter equivalent as determined in TA100, without metabolic activation.

[b]Each of the HAA6 have their own method detection limit (MDL). <MDL means that none of the HAA6 were above their method detection limits.

[c]Percentages of TTHMs and HAA6 containing either bromide only or bromide and mixed bromochlor by-products were calculated on a weight basis.

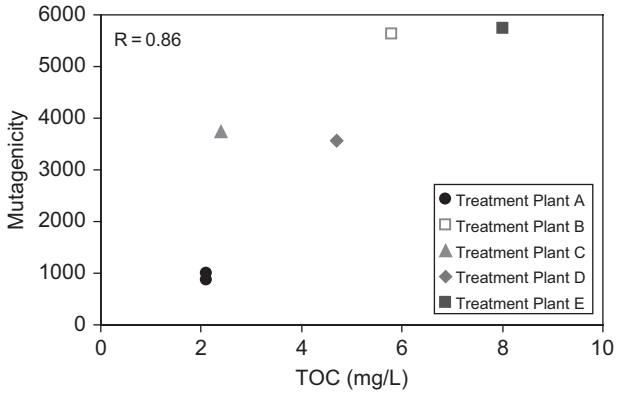

FIG. 1. Correlation between mutagenicity of the finished waters and the TOC concentrations in the raw waters.

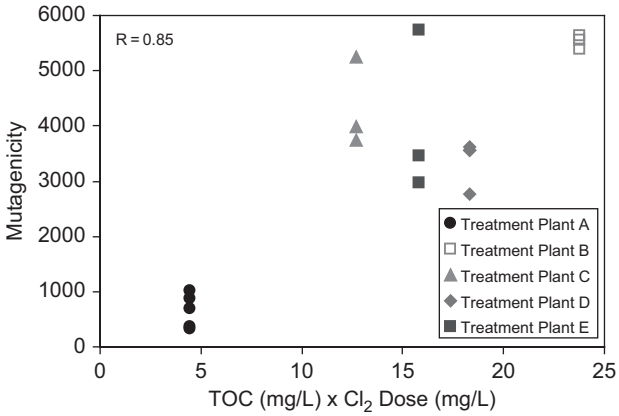

FIG. 2. Correlation between mutagenicity of the treated waters and the product of TOC of the raw waters and chlorine doses.

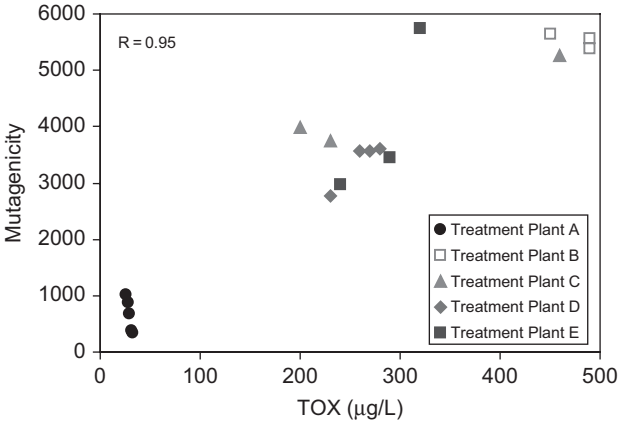

FIG. 3. Correlation between mutagenicity and TOX concentrations in the treated waters.

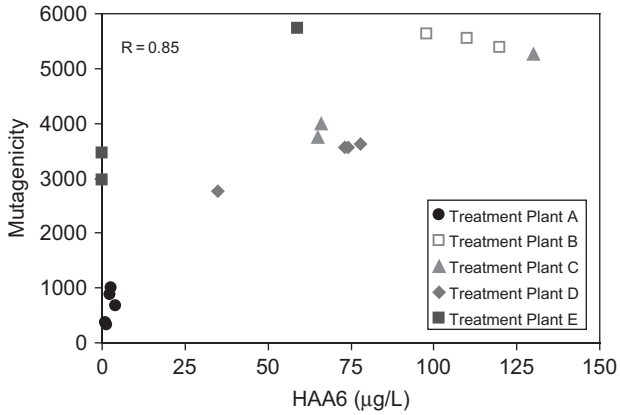

FIG. 4. Correlation between mutagenicity and haloacetic acid (HAA6) concentrations in the treated waters.

if not for the two distribution samples from plant E that had HAA6 concentrations below the detection limits, yet their mutagenicity levels were in the range of 3000 revertants/L equivalent of water. One possible explanation for the observed loss of HAA6 in these distribution samples is provided by reports that some of the HAAs are biodegradable in the absence of residual disinfectant (Baribeau et al., 2000). Neither of these samples had a detectable free chlorine residual, and both samples showed greater than a 10-fold increase in the number of heterotrophic bacteria relative to the finished water, as determined by enumeration on plate count agar. The occurrence of biodegradation in the distribution system of plant E is further indicated by the reduction in the level of assimilable organic carbon (AOC) in the distribution samples relative to that in the finished water (173 and 132 µg carbon equivalents/L and 1092 µg carbon equivalents/L, respectively).

The concentrations of the TTHM showed less of a correlation with the levels of mutagenic activity in the treated water samples than HAA6 (Figure 5). These results are consistent with those reported by Vartiainen et al. (1988) for 28 drinking water samples (r = .63). The absence of a high level of correlation between TTHM and mutagenicity might be expected, given that the formation of TTHM rise as the pH increases (Fair, 1995), whereas most of the mutagenic activity is associated with acidic/neutral chlorination by-products (Vartiainen and Liimatainen, 1986; Ringhand et al., 1987).

When bromide ions are present in the source water, the formation of brominated and mixed bromochloro by-products is favored over the formation of the chlorinated species (Fair, 1995; Clark et al., 2001). The presence of bromide may also exert a significant impact on the levels of mutagenicity observed in chlorinated drinking waters since many brominated compounds are more mutagenic than the corresponding chlorinated compounds. The levels of mutagenicity produced during the chlorination of humic acids were found to rise with addition of increasing levels of bromide by Meier et al. (1985).

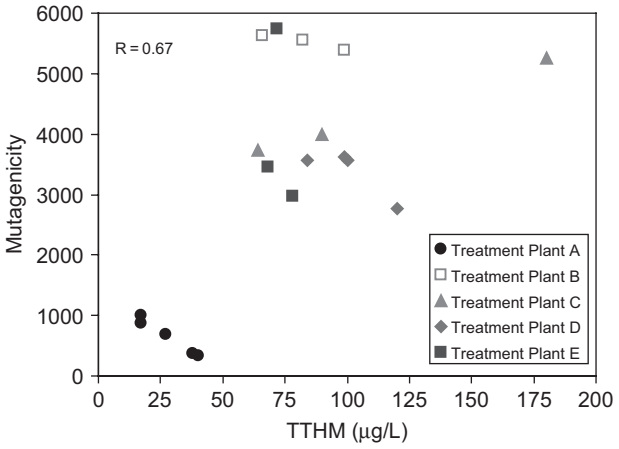

FIG. 5. Correlation between mutagenicity and TTHM concentrations in the treated waters.

In this study, four of the treatment plants had either nondetectable levels or relatively low levels of bromide in their raw waters (Table 1). Raw water from plant A, unfortunately, was not initially analyzed for bromide. However, the raw water was sampled and analyzed at a later date due to the large number of brominated DBPs observed. The bromide level at that time was 0.15 mg/L. Correlations between the levels of mutagenicity and the levels of brominated DBPs, estimated by percentages (based on weights) of TTHM and of HAA6 containing either bromide only or bromide and mixed bromochloro by-products (Table 1) all displayed negative *r* values. The absence of an increase in the levels of mutagenicity associated with the presence of bromide in this study may be due to the fact that only plant A, which used a groundwater, had bromide present. The lower levels of mutagenicity observed at plant A may merely reflect the overall lower concentrations of DBPs produced (see TOX, Table 1), relative to those observed in the surface water plant samples. The differences in the concentrations of DBPs produced in the ground water plant compared to those in the surface-water plants may be due to differences in the precursor materials present.

CONCLUSIONS

Although the data presented here were obtained from only five drinking-water treatment plants, several correlations between the formation or presence of mutagenic compounds and various water quality parameters were evident. The relationship between the formation of mutagenic compounds and the concentrations of organic precursor material (TOC) in the source water and the chlorine dose could readily be seen in this data set. The highest correlation observed in the treated water samples was between TOX and mutagenicity (mean revertants/L equivalent). A high correlation was also observed between the concentrations of HAA6 and mutagenicity in the treated water samples.

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